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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,885	01/06/2006	Weihong Xie	0643418	8347

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EXAMINER	
KASSA, TIGABU	
ART UNIT	PAPER NUMBER
1619	
MAIL DATE	DELIVERY MODE
06/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,885	XIE ET AL.	
	Examiner	Art Unit	
	TIGABU KASSA	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-17 are pending. Claims 1-12 are under consideration in the instant office action. Claims 13-17 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claims.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119 (a)-(d).

Information Disclosure Statement

The information disclosure statements (IDSs) submitted on 11/20/06 and 10/06/06 are noted and the submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the references.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness

The rejection of claims 1-12 under 35 U.S.C. 103(a) as being unpatentable over Gai et al. (CN1273114) in view of Su et al. (US Patent 4,968,675) is maintained.

Applicant Claims

Instant claim 1 recites at intravenous injection comprising saponin, iso-osmotic solution, pH stabilizer, and water at the specified concentrations. Instant claim 2-4 recite the injection of claim 1, 2 and 3, respectively, wherein the concentration of saponin is as specified. Instant claim 5 recites the injection of claim 1 wherein said iso-osmotic is sodium chloride, glucose, or sorbito l. Instant claim 6 recites the injection of claim 1, 2, 3, or 4 wherein the iso-osmotic is sodium chloride. Instant claim 7-8 recites the injection of claims 6 and 7, respectively wherein the sodium chloride concentration is as specified. Instant claim 9 recites the injection of claims 1, 2, 3, 4, or, 5 wherein the pH stabilizer is sodium citrate, citrate, phosphate, or acetate. Instant claim

10 recites the injection of claim 9 wherein the pH stabilizer is sodium citrate. Instant claims 11 and 12 recite the injection of claims 10 and 11, respectively, wherein the concentration of sodium citrate is as specified.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Gai et al teach an injection containing saponin powder of notoginseng, and water wherein the pH is regulated (abstract).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Gai et al do not teach the inclusion of an iso-osmotic. Gai et al do not teach how the pH of the injection is regulated. Gai et al do not specify concentration of the components. These deficiencies are cured by Su et al.

Su et al teach a parenteral pharmaceutical composition comprising an active ingredient, citric acid, sodium citrate, sodium chloride, and water (column 1, lines 38-49). The concentration of sodium citrate is 0.05-6.4 mM (column 1, line 45). The examiner calculates that this corresponds to a sodium citrate concentration of 0.0118-1.5 mg/ml assuming disodium citrate. The sodium chloride concentration is 3-5 mg/ml (column 1, line 46). The sodium citrate/citric acid is used to optimize pH and the sodium chloride is used to optimize osmolality of the composition (column 1 line 66-column 2 line 2).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art to stabilize the pH a pharmaceutical composition for intravenous injection using, e.g., sodium citrate, because it is a known physiological buffer. Optimization of the concentration of the buffer is within the purview of the skilled artisan. The skilled artisan would have been motivated to buffer the pH because unbuffered parenteral pharmaceutical compositions can cause hemolysis (Su et al., column 1 lines 61-63). The skilled artisan would have had a reasonable expectation of success because Su et al. teach the use of sodium citrate to buffer the pH of a parenteral pharmaceutical composition. (column 1, lines 61-63)

It would have been prima facie obvious to one of ordinary skill in the art to include an iso-osmotic in a parenteral pharmaceutical composition because the osmolarity of the aqueous pharmaceutical composition might otherwise be significantly lower than blood. Optimization of the concentration of the iso-osmotic is within the purview of the skilled artisan. The skilled artisan would have been motivated to adjust the osmolarity of the parenteral pharmaceutical composition using, e.g., sodium chloride in order to avoid hypotension (Su et al., column 1 line 65-column 2, line 2). The skilled artisan would have had a reasonable expectation of success because Su et al. teach the use of sodium chloride to adjust the osmolarity of a parenteral pharmaceutical composition (column 1 line 65-column 2, line 2).

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Applicants Remarks

Applicants first assert that the examiners rejection in the previous office action dated 12/23/2008 lacked the rational underpinning required for rejections of obviousness. The applicants are directed to the examiners arguments provided in both this and the previous office action under the section entitled "Finding of Prima Facie Obviousness Rational and Motivation." Applicants also assert that there is no basis for turning to the teachings of Su et al. to address the deficiencies of Gai et al. Specifically, the applicants' remarks relate to pH. As applicants and the examiner have both pointed out, Gai et al. teach the regulation of pH, although the means and the final pH are not cited. Therefore, even without the teachings of Su et al., the regulation of pH is known and taught by Gai et al. Use of a physiological buffer for such a regulation would be obvious to the skilled artisan since the composition of Gai et al. is designed for injection. Although the compound taught by Su et al. is not the same as the instantly claimed compound (i.e. the compound taught by Gai et al.), it is sufficiently similar as to provide valuable and relevant guidance to the skilled artisan in determining the types and amounts of buffers to use. Moreover, the teachings of Su et al. also lead the skilled artisan to include sodium chloride to adjust the osmolarity. The examiner notes that applicants offer no remarks related to the formation of an iso-osmotic solution except to point out that the composition of Su et al. still caused hypotension. The examiner notes that Su et al. only mention hypotension with regard to cats although the solution was also tested in dogs and monkeys. Therefore, in the majority of mammals tested, the composition was satisfactorily iso-osmotic. Since the serum composition of many mammals are known, further optimization to tailor the composition to specific species is obvious and within the purview of the skill artisan. Moreover, since the instantly claimed

invention does not specify a single species with respect to which the composition must be iso-osmotic, a composition which is iso-osmotic to at least one species of animal is sufficient to support the conclusion of obviousness. Applicants point out that the pH disclosed by Su et al. is 3.0 and state that this is different from the pH in the instant application. However, the pH value is not an instantly claimed limitation. Additional components such as the acid used by Su et al. to adjust the pH are not precluded in the instantly claimed invention since instant claim 1 is worded as "comprising." The examiner further notes that the optimization of pH is within the purview of the skilled artisan and is, therefore, both obvious and reasonably expected to succeed. The teachings of Su et al. provide sufficient guidance to the skilled artisan to add appropriate a physiological buffer and sodium chloride to the composition of Gai et al. since the compounds taught by Gai et al. and Su et al. are related steroid derivatives. By simply optimizing the pH and concentrations of buffer and salt, the skilled artisan would obtain the instantly claimed invention.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Claims 1-12 are rejected. Claims 13-17 are withdrawn. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIGABU KASSA whose telephone number is (571)270-5867. The examiner can normally be reached on 9 am-5 pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tigabu Kassa 6/13/09

/Mina Haghighatian/
Primary Examiner, Art Unit 1616